

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 19 MAY 2006

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Applicant's or agent's file reference LHPB60727		FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/EP2005/001449		International filing date (day/month/year) 10.02.2005		Priority date (day/month/year) 14.02.2004
International Patent Classification (IPC) or national classification and IPC INV. C07D473/04 C07D473/06 A61K31/522 A61P9/00 C07D473/00				
Applicant SMITHKLINE BEECHAM CORPORATION				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 13.12.2005		Date of completion of this report 19.05.2006		
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized officer De Jong, B Telephone No. +31 70 340-2833		



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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-65 as originally filed

Claims, Numbers

1-17 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 12,13 (with respect to industrial application)

because:

- ☒ the said international application, or the said claims Nos. 12,13 (with respect to industrial application) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	13,15-17
	No: Claims	1-12,14
Inventive step (IS)	Yes: Claims	
	No: Claims	1-17
Industrial applicability (IA)	Yes: Claims	1-11,14-17
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

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Re Item III.

Claims 12,13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

Reference is made to the following documents:

- D1 : EP 0 389 282 A (BEECHAM - WUELFING GMBH & CO. KG; BEECHAM GROUP P.L.C; SMITHKLINE BEEC) 26 September 1990 (1990-09-26)
- D2 : WO 92/09203 A (SMITHKLINE BEECHAM CORPORATION) 11 June 1992 (1992-06-11)
- D3 : WO 99/20280 A (SMITHKLINE BEECHAM CORPORATION; GRISWOLD, DON, E; CHRISTENSEN, SIEGFRI) 29 April 1999 (1999-04-29)
- D4 : WO 93/16699 A (SMITHKLINE BEECHAM CORPORATION) 2 September 1993 (1993-09-02)
- D5 : ARCH, JONATHAN R. S. ET AL: "Inhibition of type 4 cyclic nucleotide phosphodiesterase by 8-chloroxanthines" ARCHIV DER PHARMAZIE (WEINHEIM, GERMANY) , 329(4), 205-208 CODEN: ARPMAS; ISSN: 0365-6233, 1996, XP008046719
- D6 : JACOBSON, KENNETH A. ET AL: "Effect of trifluoromethyl and other substituents on activity of xanthines at adenosine receptors" JOURNAL OF MEDICINAL CHEMISTRY , 36(18), 2639-44 CODEN: JMCMAR; ISSN: 0022-2623, 1993, XP002327691
- D7 : SMELLIE, F. W. ET AL: "Alkylxanthines: inhibition of adenosine-elicited accumulation of cyclic AMP in brain slices and of brain phosphodiesterase activity" LIFE SCIENCES , 24(26), 2475-81 CODEN: LIFSAK; ISSN: 0024-3205, 1979, XP008046723
- D8 : KATTUS, ALBERT A. ET AL: "Diuretic activity of compounds related to xanthines, uracils, and triazines as determined in dogs" BULLETIN OF THE JOHNS HOPKINS HOSPITAL , 89, 1-8 CODEN: JHHBAI; ISSN: 0097-1383, 1951, XP008046730

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1) The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-12,14 is not new in the sense of Article 33(2) PCT:

D1 discloses pharmaceutical compounds of formula (I), according to claims 13 in D1. These compounds are useful in treating e.g. cardiovascular diseases. This teaching is novelty destroying for claims 1-12,14 of the present application. The specific compounds according to examples 15,16 are novelty destroying for claim 11. Contrary to what is said in the applicants letter of 13.12.2005 claim 11 of the present application is not a second medical use claim.

D2 discloses TNF inhibitors of formula (I), according to claim 1. This generic teaching is novelty destroying for claims 1-12 of the present application. Some of the specific compounds according to claim 11 (and their use) are novelty destroying for claim 11 of the present application.

D6 discloses compound 28, which has adenosine receptor activity. This teaching is novelty destroying for claims 11,14 of the present application. The argument in the applicants letter of 13.12.2005 that there is no teaching from D6 to use compound 28 in medicine is incorrect, since this a pharmaceutical effect of this compound is disclosed in D6.

Documents D3, D4 are novelty destroying for claims 1-11 of the present application.

Document D7 discloses the 8-bromo-xanthine derivative in Table 1, which is novelty destroying for claim 11.

Document D8 discloses the compound 1,3-diehyl-8-bromoxanthine in Table 1, which is novelty destroying for claim 11.

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2) The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-17 does not involve an inventive step in the sense of Article 33(3) PCT:

There is no basis for acknowledging inventive step for claims which are not novel. It is however noted that the compounds according to claim (I) in which R3 is CN are considered as novel and inventive.

Claims 15-17 can only be considered as inventive in combination with inventive compound claims.

3) The application does not meet the requirements of Article 6 PCT, because claims 1,11 are not clear:

The term "physiologically functional derivative thereof" makes the scope of the claims unclear.

4) For the assessment of the present claims 12,13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims.